B) DNA comprising the sequence:

GAT AGT GTG TGT CCC CAA GGA AAA TAT ATC CAC CCT CAA
AAT AAT TCG ATT TGC TGT ACC AAG TGC CAC AAA GGA ACC TAC
TTG TAC AAT GAC TGT CCA GGC CCG GGG CAG GAT ACG GAC TGC
AGG GAG TGT GAG AGC GGC TCC TTC ACC GCT TCA GAA AAC CAC
CTC AGA CAC TGC CTC AGC TGC TCC AAA TGC CGA AAG GAA ATG
GGT CAG GTG GAG ATC TCT TCT TGC ACA GTG GAC CGG GAC ACC
GTG TGT GGC TGC AGG AAG AAC CAG TAC CGG CAT TAT TGG AGT
GAA AAC CTT TTC CAG TGC TTC AAT TGC AGC CTC TGC CTC AAT
GGG ACC GTG CAC CTC TCC TGC CAG GAG AAA CAG AAC ACC GTG
TGC ACC TGC CAT GCA GGT TTC TTT CTA AGA GAA AAC GAG TGT
GTC TCC TGT AGT AAC TGT AAG AAA AGC CTG GAG TGC ACG AAG
TTG TGC CTA CCC CAG ATT GAG AAT; and

C) a fragment of A or B.--

REMARKS

Applicants canceled claims 10, 12, 14, 17, 18, and 22 without prejudice or disclaimer. Applicants amended claims 2 to 6 and 11. Applicants added claims 27 to 61. Claims 2 to 7, 9, 11, 23, and 27 to 61 are presently pending.

The Examiner rejected claims 7, 14, 18, and 23 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled. Office Action at page 2, line 15, to page 4. The Examiner contended that claim 7 is beyond the scope of the disclosure "because there is no teaching in the specification what part of the TNF-BP is responsible for binding to TNF," and one skilled in the art could not predict the "part of the TNF-BP encoded by the DNA of claim 2 [that] will retain TNF binding function." Id. at page 2, lines 23 to 28. In view of the alleged unpredictability, the Examiner contends that undue

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experimentation would be required to determine portions of the TNF-BP that retain activity. Id. at the sentence bridging pages 3 and 4.

The Examiner further contends that the disclosure does not enable claim 7 since it encompasses nucleic acids encoding "an extracellular domain of undisclosed TNF receptors, for example." Id. at page 3, only full paragraph. The Examiner contends that "[i]t would require undue experimentation to predict and prepare the binding proteins encompassed within the scope of the claims that possess the desired and favorable characteristics set forth in the specification, in the absence of sufficient information to predict the results with an adequate degree of certainty." Id. (citation omitted).

The Examiner also contends that the claimed nucleic acid must hybridize to a DNA complementary to a portion of the DNA of claim 2 that encodes a portion of TNF-BP that retains the ability to bind to TNF. Id. at the paragraph bridging pages 3 and 4. The Examiner correctly notes that claim 7 is directed to nucleic acid that encodes a polypeptide that has the ability to bind to TNF. Id. at page 4, last paragraph. In other words, the nucleic acid of claim 7 hybridizes with a DNA complementary to the DNA defined in claim 2, rather than with the DNA defined in claim 2.

Finally, the Examiner contends that the low stringency is undefined and "[a]t low stringency conditions for hybridization[,] the actual identity between the DNA can be very low and encode different proteins." Id.

Applicants respectfully assert that the Examiner has not established that one skilled in the art, in view of the present specification, could not determine portions of the

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claimed nucleic acid that encode polypeptides that have the ability to bind to TNF. First, the Examiner appears to agree that the entire sequence of claim 2 encodes a polypeptide that has the ability to bind to TNF. Since the nucleic acid of claim 7 hybridizes to a DNA complementary to the DNA defined in claim 2, claim 7 includes nucleic acid having the entire DNA of claim 2 and fragments of that DNA that encode a polypeptide having the ability to bind to TNF. Applicants respectfully assert that it would not require undue experimentation for one skilled in the art to test portions of that polypeptide sequence to determine whether they retain the ability to bind to TNF. Predictability in advance is not required if the experimentation merely requires the time to make portions and test them for activity using routine tests. The Examiner has failed to address the type of experimentation involved and the high level of skill in the art. Without addressing such other factors, such as those set forth in In re Wands, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988), the Examiner fails to establish a *prima facie* case that undue experimentation would be required to find nucleic acids encoding polypeptides that have the ability to bind to TNF.

Also, applicants note that it is not required that the nucleic acid of claim 7 hybridize to a DNA complementary to a portion of the DNA of claim 2 that encodes a polypeptide having the ability to bind to TNF. Although the nucleic acid of claim 7 itself must encode a polypeptide having the ability to bind to TNF, there is no limitation on the portion of the DNA of claim 2. The Examiner apparently had misconstrued claim 7 in this respect. To expedite prosecution, claim 7 has been amended to further clarify this point.

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Second, the Examiner has not established that the specification does not enable nucleic acids of claim 7 other than the entire sequence of claim 2 or fragments of it. At the outset, applicants assert that the Examiner has failed to establish that the term "low stringency" in claim 7 is undefined. Although researchers may employ varying conditions, applicants assert that one skilled in the art would understand that "low stringency" conditions are those in which a positive signal is detectable above the background. Applicants assert that one skilled in the art would be able to vary conditions such as incubation temperature, salt concentration, and buffer to obtain the desired result of selecting over background. Applicants attach a copy of Shimuzu et al., PNAS USA, 80:2112-2116 (1983), which discusses the concept of low stringency hybridization (see, e.g, Shimuzu at page 2112, second column, penultimate paragraph).

Next, the Examiner's concern that unrelated nucleic acids would be encompassed by claim 7 is not founded. It should be clear that conditions in which many different unrelated sequences hybridize is not what is intended by "low stringency" conditions as set forth in claim 7. In fact, claim 7 requires that the claimed hybridizing nucleic acid code for a polypeptide having the ability to bind TNF.

As applicants have previously asserted, one skilled in the art could use routine tests to determine if the encoded polypeptides have the ability to bind to TNF.[1] The Examiner has not addressed the routine nature of the testing or the high level of skill in

[1] Applicants continue to rely upon the assertions advanced in the Response filed on November 22, 1995, including the assertions on this point at page 3, first full paragraph, through page 4, third paragraph.

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the art. Applicants respectfully assert that the proper enablement standard does not require the ability to predict in advance with an adequate degree of certainty. A standard that requires one to predict results in advance with an adequate degree of certainty would remove the well established precedent that permits experimentation for enablement.

For all of these reasons, applicants respectfully traverse this § 112, first paragraph, rejection, and request reconsideration and withdrawal of it.

The Examiner rejected claims 7, 14, 18, and 23 under 35 U.S.C. § 112, second paragraph, as allegedly not being enabled. Office Action at page 5. The Examiner contended that it is unclear whether claim 7 requires the claimed nucleic acid or the DNA of claim 2 to encode a polypeptide having the ability to bind TNF. Although applicants assert that claim 7 as previously drafted was clear on this point, they have amended claim 7 to make the invention even more clear. Accordingly, this rejection under § 112, second paragraph, is moot.

Applicants acknowledge the Examiner's statement that claims 2 to 6, 9 to 12, 17, and 22 are allowable over the prior art of record.

If there are further fees due in connection with the filing of this Amendment, such as fees under 37 C.F.R. §§ 1.16 or 1.17, please charge the fees to our Deposit Account No. 06-0916. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested. This fee also should be charged

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to our Deposit Account No. 06-0916. Any overpayment may be credited to Deposit Account No. 06-0916.

Respectfully submitted,

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